Usability of the software MacuFix for the categorization of metamorphopsia and evaluation of patient adherence compared to the Amsler Grid

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Abstract

Aim: Macular diseases can lead to metamorphopsia, which is traditionally tested using the standard functional test, Amsler grid. The current study attempts to evaluate a new method to assess metamorphopsia, which is based on the software AMD-A Metamorphopsia Detector, the app MacuFix®.

Methods: In this observational study, the usability of a new smartphone-based testing method to assess metamorphopsia was evaluated in 45 patients experiencing metamorphopsia in at least one eye using the questionnaire "System Usability Score (SUS)". Additionally, the diagnostic adherence of self-monitoring with the Amsler grid was compared to self-monitoring with the novel software MacuFix®.

Results: The average score of the SUS questionnaire in this study was 76.7 (SD=±15.5) corresponding to the score "excellent". The average interval between two home tests was significantly shorter when using the app MacuFix (6 days) compared to using the Amsler grid (19 days). Once the app was available, the odds ratio for persons previously not using a home test to imply the app as a home test was 4.5.

Conclusion: MacuFix® application can help meet the unmet needs in home monitoring of macular function as high user satisfaction and increased testing frequency was observed with the use of MacuFix®. This may lead to improved outcomes in the treatment of macular disease.

Key Words:

Metamorphopsia, Usability, Adherence, Age-related macular degeneration
Diabetic macular edema, Smartphone-based app

Introduction

Diseases of the macula can lead to metamorphopsia traditionally tested with the Amsler grid as the standard functional test.[1] Alternative tests are supposed to overcome its limitations.[2-6] A new method to assess metamorphopsia is based on the software AMD-A Metamorphopsia Detector®.[7,8] The MacuFix® test (app4eyes, developed by Ronald Krüger, patent DE 10 2019 205 318 A1) is available for use on a screen (PC, smartphone, tablet, iPad) both for Android and iOS platforms. This study determined the user-friendliness with the questionnaire "System Usability Score (SUS)" and compared the adherence of self-monitoring with the Amsler grid versus the software MacuFix®.[9,10]

Materials and Methods

For this observational pilot study 47 persons were recruited from the patient pool of an ophthalmologic group practice and subjected to the study examination as part of their medically necessary control examination.

As early as October 2019, patients were informed about the planned study and that inclusion in the study could only take place after a positive vote of the ethics committee. In the context of the Covid-19 pandemic, stakeholders recommended to reduce the number of follow up visits. Many of those interested in participating in the study asked for a home test as a supplement to conventional diagnostic tests such as Optical Coherence Tomography (OCT). For this reason, based on the approval of the competent ethics committee (No. 600213225), the decision was made to inform the participating persons about the possibility of using the App MacuFix® as a home test

and to start a prospective, controlled study to examine the adherence using a self-test. After a positive vote by the Ethics Committee of the North Rhine Medical Association (No. 2020057) on 1st April, 2020, in which the Ethics Committee stated that there were no professional ethical or legal objections to the study, patients who had expressed interest in participating in the study were informed about the study in writing. After signing informed consent 45 patients were included in the study from 4th May, 2020 – 30th June,2020. The study conformed to the tenets of the Declaration of Helsinki of 1975, as revised in 2013.

Inclusion criteria

Patients aged above 18 years of either gender with metamorphopsia (ICD Code H 53.15) in at least one eye, detected with Amsler grid and a best-corrected visual acuity (BCVA) of at least 20/200 and consenting to participate in the study were enrolled.

Exclusion Criteria

Patients not fulfilling the inclusion criteria, advanced glaucoma and intraocular surgery other than cataract surgery or vitrectomy within prior 3 months could not participate in the study.

Endpoints

The primary endpoint investigated in the observational study was the score of the SUS questionnaire. The secondary endpoint investigated in the prospective, controlled interventional study arm was the frequency of use of the Amsler test or the app MacuFix® measured as the time interval in days between two measurements to assess test adherence.

Examination procedure and period

As part of a routine examination, each participating patient carried out the MacuFix test with each eye with adequate near correction once in the period 4th May, 2020 –

30th June,2020. In addition, BCVA was measured, a retinal examination was performed and a spectral domain OCT (SD-OCT, CIRRUS ™ HD-OCT, Carl Zeiss Meditec) was performed. All study patients filled out the pseudonymised questionnaire SUS after performing the MacuFix® test. If they were interested, the patients were given a link for free use of MacuFix® as a home test on a PC for future use of the test. Alternatively, the patients could download the test as an app for use with an iPad or smartphone. The patients were asked whether they agreed to be interviewed about the frequency of the Amsler test and after three months about the frequency of using the app or the Amsler grid.

On the study day, each patient was asked about the frequency of use of the Amsler test. The standardized question was: "I would like to know from you how often you have used the Amsler Grid in the past. The following question refers to the period from January 2020 to March 2020 (baseline period): How many days usually elapsed after a test with the Amsler Grid until the next test?"

12-14 weeks after the study day, patients were contacted by telephone and asked about their testing behavior during the previous three months (comparison period). The standardized question was now: "I would like to ask you two questions about the Amsler Grid and the App Macufix®. With my question I would like to record how often you have carried out one of the two tests in the past three months. Did you use one of the two test methods?" The following question, if applicable was "How many days usually elapsed after a test with the method you chose until the next time you used this test method?"

Explanation of the test procedure for the MacuFix® Test

The interactive test shows on a PC screen four square fields with a grid pattern of horizontal and vertical lines. All four fields have lines that are partially distorted

(wavy). However, one of the four squares differ from the remaining three squares by more strongly distorted lines (see Figure 1). The difference between this grid pattern and the remaining three can be noticeable or small. The task of the test patient is to select this more distorted field when viewing with one eye wearing appropriate near correction. The selection can be made by pointing or a verbal message for an assistant or by tapping on the touch screen. This selection must be made at least 10 times per eye to reach a result: an algorithm determines the smallest distortion difference that was correctly named in at least 80%. This is given as a class, where class 1 stands for the smallest distortion difference offered, i.e. the best result. The procedure takes about 2 minutes per eye. Encrypted results can be sent to the ophthalmologist via email. Afterwards the other eye is tested in the same way. All data remain on the device during the MacuFix® test. The test was developed in accordance with the German data protection regulations (DSGVO).

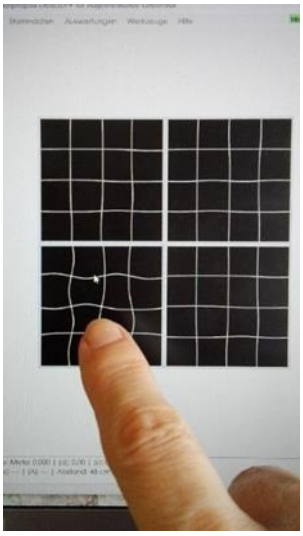

Fig. 1 MacuFix® Test on a mobile device

System Usability Scale (SUS) Questionnaire

The SUS questionnaire was developed to determine how users perceive the ease of use of a software.[10] It consists of ten statements based on Likert scale, each with

five possible answers ranging from complete rejection to complete agreement. The SUS questionnaire contains five positive and five negative statements about the usability of the system to be evaluated. Thus, data is collected which can be quantitatively evaluated and interpreted, the result is a percentage usability value of the application. The SUS questionnaire contains the following ten statements:

- I can well imagine using the test regularly.
- I find the test unnecessarily complicated.
- I find the test easy to use.
- I think I would need technical support to use the test.
- I find that the various functions of the test are easy to use.
- I think that there are too many inconsistencies in the test.
- I can imagine that most people learn to master the test quickly.
- I find the operation very complicated.
- I have felt very confident in using the test.
- I had to learn a lot of things before I could work with the test.

For each statement the participant gives his agreement or disagreement in the form of a scale ranging from 1= strong agreement to 5= strong disagreement. The results of the SUS questionnaire are used to calculate a numerical value (the SUS score). The categories in the SUS questionnaire are coded with values from 0 to 4. The coding depends on the formulation: If the answer is positive, the answer will be coded as 4 for full agreement and 0 for a complete rejection. If the answer is negative, the answer will be coded as 0 for full agreement and 4 for a complete rejection. The numbers obtained in the 10 questions are added together - the sum is between 0 and 40 - and then multiplied by 2.5. For example, if the sum of all answers is 22, the SUS

score is 55. The results of the SUS questionnaire range from 0 (worst score) to 100 (best score).

Survey on test frequency

As part of the study investigation on the study day, the study participants were asked how many days had usually elapsed between two Amsler grid tests in the baseline period. The response spectrum could range from "1" for daily performance to "90" for a maximum of once in three months. 12-14 weeks after the study day, the study participants were called and asked how many days elapsed between the performance of two self-tests in the previous 3 months (comparison period).

Statistical Analysis

Since the study had a primarily exploratory character, no a priory sample size was carried out. The study had two groups of patients, the group of patients who continued to use the Amsler test or no selftest after the study day (group “Stay”) and the group of patients who used the app MacuFix® after the study day (group “Switch”).

Comparison "Stay" and "Switch" after the study day

For the prospective, controlled study on adherence using a self-test, the null hypothesis was, there is no difference in the mean values of the two populations with respect to the frequency of use of the Amsler grid and the MacuFix® software (interindividual comparison using t-test for unrelated samples). The alternative hypothesis was, there is a difference in the mean values of the two populations.

Intraindividual comparison of the test frequency before and after the study day in the "Stay" and "Switch" group

The null hypothesis for the intraindividual comparison was: the frequency of use changed in the group of patients who stayed with the Amsler grid in the same way as those who switched to the MacuFix® test (intraindividual comparison using the t-test for paired samples). The alternative hypothesis was, the change in test frequency was different in the group of patients who stayed with the Amsler grid compared to those who switched to the MacuFix® test.

Comparison of "Stay" and "Switch" before the study day

In addition, the t-test for unrelated samples was used to compare whether the "Stay" group differed from the "Switch" group in the frequency of self-testing prior to the study day in order to rule out a selection bias. The statistical method used for this intraindividual comparison was the two-sided t-test for paired samples.

All statistical analyses were performed with the statistical software "R" (Version 3.6.1., R Foundation, R Core Team): A Language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. http://www.R-project.org).

Results

Composition of the investigated collective

Of 75 patients questioned, 47 were willing to participate in the study. One patient withdrew her consent and one patient was unable to participate in the study due to the treatment of a glioblastoma, which had become apparent before the study day through a scotoma on the functionally single eye. The remaining 45 patients (18 females, 27 males) completed the SUS questionnaire on the same day after the

MacuFix® test had been performed and answered the question referring to the test frequency of the Amsler test in the baseline period. Thirty-five study participants were interested in using the MacuFix® test as a home test after the study, three of them used a PC, one patient used an iPad and 31 used a smartphone. All subjects agreed to a telephone survey to be conducted later on the frequency of using a home test.

The mean age was 68 ± 9.7 years (SD). The mean visual acuity was 20/30 (Snellen fraction) or 0.6 (decimal) respectively (SD=0.25). Of the 90 eyes, 18 eyes showed no abnormal macular findings. In 22 eyes, there was an early macular degeneration with small to medium sized drusen but no changes in the retinal pigment epithelium. Sixteen eyes showed intermediate age-related macular degeneration (AMD) with large drusen or at least medium-sized drusen associated with pigment epithelial changes. Fourteen eyes suffered from AMD (four geographic atrophy, ten neovascular AMD). In six cases, epiretinal gliosis or vitreo-macular traction was present. One eye showed a macular hole. Diabetic macular edema (DME) was present in both eyes of one patient. In one eye macular edema was due to retinal vein occlusion, in two eyes due to uveitis. Two eyes showed no edema after treatment for uveitic edema. Four eyes had developed Irvine Gass Syndrome 4-12 weeks (average 7.5 weeks) after cataract surgery while two eyes had central serous chorioretinopathy. Of the 90 eyes of 45 study participants two eyes could not be measured with Macufix due to central scotoma caused by geographic atrophy. MacuFix measurements of 88 eyes were included.

Sensitivity and Specificity of MacuFix to identify Metamorphopsia

When examined with the Amsler Grid, 42 eyes perceived metamorphopsia, 46 did not see metamorphopsia. Referring to the Amsler Grid as a gold standard, MacuFix® measurements were correct positive in 38, false positive in four, correct negative in 43 and false negative in three cases. This led to a sensitivity of the App MacuFix® of 92.7% and a specificity of 91.5 %.

Score SUS

Average values of the individual questions in the SUS questionnaire are enlisted in Table 1. 0 corresponds to a negative and 4 to the best possible rating. The app received the best ratings in questions number 7,8,10 reflecting that the study participants experienced the test as easy to learn and uncomplicated. To illustrate the result of the SUS score, Bangor et al associated the SUS scores of 1000 questionnaires with a scale of seven adjectives.[9] The scale contains adjectives such as "good," "ok," and "bad", that users loosely associated with the usability of a product. The authors found that ratings with a score above 85 were associated with "best possible". "Excellent" corresponded to ratings of 73-84 points, "good" was associated with ratings whose score was 63- 72 points. The rating "okay" correlated with score values from 52- 63 and the rating "poor" was associated with score values of 51 or less. The average score of the SUS questionnaire in this study was 76.7 (SD=±15.5), which corresponds to the score "excellent".

Choice of the test procedure

Of 38 persons who used the Amsler test in the baseline period, eight persons continued using the Amsler grid in the comparison period (group “Stay”). The remaining 30 patients decided to use the MacuFix test instead of the Amsler test (group “Switch”).

Seven of the 45 patients had not used any self-test to check for metamorphopsia in the baseline period. Two of them continued not to use a self-test in the three month comparison period after the study day. The remaining five patients used the MacuFix® app in the comparison period. None of these patients used the Amsler grid after the study day.

Test Frequency

The average interval between two Amsler tests was 22.5 days in the baseline period (SD = ±14.1; confidence interval (CI) = 18.1; 27.0). The average interval between two Amsler tests in the comparison period was 19.4 days (SD = ±10.8; CI = 11.9; 26.9). The average interval between performing two MacuFix tests after the study day was 5.8 (SD = ±6.4; CI = 3.7; 7.9).

Intra-individual comparison in the group that continuously used the Amsler test ("Stay")

In this group, the interval between two Amsler tests averaged 26 days in the baseline period from January to March 2020 and 19 days between two Amsler tests in the three month comparison period after the study day. In the group "Stay" the critical value is 2.365 with seven degrees of freedom and a probability of error (α) = 0.05. Since the test statistic of 1.697 is not higher than the critical value, the test frequency with the Amsler test in the baseline period did not differ significantly from the comparison period (t-test for paired samples: ($|-1.697| < 2.365$; $p > 0.05$; $n = 8$).

Intraindividual comparison in the group that switched from the Amsler test to App MacuFix ("Switch")

In this group the test frequency increased statistically significant after switching from Amsler grid to MacuFix. The time interval between two Amsler tests averaged 31 days in the baseline period. In the comparison period the average interval between two MacuFix tests was 6 days.

In the Switch group, the critical value is 2.032 at 35 degrees of freedom and $\alpha = 0.05$. Since the test statistic of 6.135 is higher than the critical value, the difference is significant (t-test for paired samples: $(|-6.135| > 2.032; p < 0.001, n = 36)$.

Interindividual comparison of the test frequency in the Amsler group with that in the MacuFix group after the study day

The Welch test was chosen because of the different sample sizes. In the comparison period the average time interval between two tests in the Amsler group was 19 days, whereas in the MacuFix® group the next test was performed after an average of six days. The average time to the next test was 13 days shorter in the MacuFix® group (95% CI: [3.82; 23.37]), t (7.98) =3.21). This difference was statistically significant ($p < 0.05$).

Comparison of the frequency of the Amsler test before the study day

In order to determine whether the group of patients who used the Amsler test throughout the study (group “Stay”) differed in their general self-behavior from those who switched to the App MacuFix®,(group “Switch”) the test frequency data was compared before the study day.

In the baseline period the average time interval between two Amsler tests in the "Stay" group was 26 days. In the "Switch" group, the next test was performed after an average of 31 days during the baseline period. The time to the next test showed no statistically significant difference when using the Welch test in both groups (95%-KI:

[-21.60; 10.66]), t (15.91) = -0.72; p>0.05. In the baseline period subjects who used the Amsler test continuously and those who switched to the App MacuFix® later showed no difference in their test behavior.

Test behavior dependent on gender

Six of the seven subjects who did not use a home test before the study were men. Two of these men continued not use any home tests after the study day, four of them used the MacuFix® test. Thus, 60% of the men and one woman who had not applied any home test previously, decided to use the MacuFix® test after the study day.
The group of subjects who used the Amsler test in the baseline period consisted of 18 females and 20 males. Eight female subjects from this group continued to perform the Amsler test after the study day. The remaining ten females switched to the MacuFix® test after the study, as did all 20 males in this group. Thus, in the group that had already used the Amsler test before the study, 55% of the women and 100% of the men decided to use the MacuFix® test instead of the Amsler tests for self-monitoring in the future.

Proportion of patients who did not use a home test

Prior to the study seven of 45 patients (15.5%) did not use any home test to evaluate their macular function. After the study five of these patients used the App MacuFix®, whereas two of 45 patients (4.4%) continued not to use any home test.
The odds ratio for persons previously not using a home test to imply a home test in their routine was 4.5 (OR=7/38: 2/43= 4.5) due to MacuFix®.

Discussion

The current study evaluated the comparative data of 45 patients using the application MacuFix® and the standard functional test, Amsler Grid. Regarding sensitivity and specificity, comparability of MacuFix® and the Amsler Grid, is to some extent limited, because MacuFix® tests the central 4° of the visual field whereas the Amsler Grid examines 10° when used in the intended distance.

Transferability into everyday care

According to the SUS questionnaire, the study participants found the test easy to learn and uncomplicated, which may also be due to the playful character of the app. When using the SUS questionnaire, the app received the worst score on the question no. 6 "I think there are too many inconsistencies in the test". In order to reduce barriers to implementing the intervention, the help function for using the app has been revised in the meantime with the cooperation of patients, educators and linguists and the display of the test results has been improved.

An improvement in health care through self-monitoring tools may possibly improve diagnostic and subsequently therapeutic adherence and persistence, thus leading to better maintenance of the patient's vision. Home monitoring and telemedicine using computer-based testing is especially important in resource deprived areas, for less mobile patients such as those in senior care homes or when reduced contacts are desirable, as has been highlighted by the ongoing Covid-19 pandemic.[11-14]

Amsler grid test is popular as it is inexpensive and can be easily explained to the patients for assessment of progressive macular damage. Unmet needs in home monitoring of macular function are derived from the limitations of the Amsler grid such as the non-interactive nature of the test, the missing fixation control during the test, the need for reasonable reading vision to discern the lines, a low sensitivity due

to a suprathreshold stimulus, its poor performance due to the ‘crowding effect' and limited awareness of visual field defects until the scotoma is significantly large in size due to ‘filling-in phenomenon'.[15,16]

Some of the ophthalmic home-based tests developed so far do not satisfy the needs of patients due to complicated handling and/or high purchase price and/or regulated access. These patients can either not afford, do not have access to devices for testing due to regulatory hurdles or do not want or are unable to use new technologies. The AREDS2-HOME study revealed that 20% of patients who were offered the hyperacuity-based ForeseeHome monitoring device (Notal Vision Ltd, Tel Aviv, Israel) were unable to use it successfully due to visual field defects or problems with its application. [17]

Diagnostic and therapeutic adherence are crucial for treatment persistence. Ehlken et al observed that 44% of their patients did not reveal sufficient adherence in the first year of treatment.[18] The AURA study highlighted the role that regular monitoring plays in guiding neovascular AMD (nAMD) therapy.[19] The OCEAN study showed that a timely start of therapy leads to an improved outcome, but unfortunately only 60% of patients continued the therapy after two years.[20] The POLARIS study found that the adherence of patients with DME is lower compared to AMD patients.[21] The ANDROMEDA study investigates the factors that influence the adherence in patients with AMD.[22]

Delayed diagnosis or detection of progression of metamorphopsia account for poor visual prognosis and this opens up an area of application for home monitoring and telemedicine. Pinnacle clinical trials evaluating anti–vascular endothelial growth factor (VEGF) therapies in management protocols for nAMD have demonstrated significant visual acuity gains, yet these same benefits are not always reflected in real-world patient analyses. In a systematic review, Carrasco et al. described real-

world outcomes in the treatment of AMD by intravitreally administered antivascular growth factors (anti-VEGF) and found that the amount of the visual acuity gain as seen in the studies was superior to the visual acuity gain seen in the real world settings.[23]

Angermann et al. retrospectively analyzed data of 1264 patients with diabetic retinopathy or nAMD receiving treatment with anti-VEGF between 2015 and 2018.[24] Multivariate regression analysis showed that advanced age, lack of mobility, and need for assisted transport, poor final visual acuity despite treatment, and decrease in vision during the observational period were independent risk factors for terminating the treatment. The authors concluded that taking the risk of disease progression into account, strategies for better compliance and adherence to therapy should be considered to optimize patient care. The aspect of improving adherence is crucial as well for partner eyes bearing an annual risk of conversion to nAMD of 24%.[25] The authors of the post-hoc analysis of the VIEW study requested close monitoring of these eyes at risk.[26]

Macufix® has been shown to be a reliable tool for metamorphopsia detection in AMD patients.[27] In the present study, the usability of the Macufix® App was rated as excellent and its availability increased the test frequency by a factor of 3. Therefore, we suggest that MacuFix® can safely be offered as a home monitoring solution that can connect patients or individuals at risk for macular disease with their eye care professional and thus improve patient self-management.

Limitations of the study

A selection bias may be due to the fact that study participants were recruited from our own patient pool who may have been particularly motivated to perform and rate the test positively in the sense of social desirability. An observation bias may have arisen

from the announcement and conduct of a telephone interview and thus have influenced adherence.

In the present study, a randomization was deliberately avoided, since it does not represent the everyday practice pattern: patients select a home monitoring test mainly based on their own decision and will accomplish it based on an intrinsic motivation. The allocation in the context of a randomization can falsify this picture and assign patients to a test, which they would not select of their own free will.

In diseases which result in metamorphopsia, a variety of factors such as age, experience with electronic media, visual acuity, other diseases affecting visual acuity or the visual field such as cataract or glaucoma, can influence the test adherence to an app as confounders. The risk of statistical bias was reduced in our study by intra-individual comparison.

Conclusion

Therapeutic agents and dosing strategies designed to overcome treatment burden by extending the time between dosing intervals continue to evolve and thus have the potential to improve quality of life and visual outcomes in patients with AMD, particularly nAMD, when integrated into clinical practice. To avoid discrepancies between clinical trials and real-world data due to undertreatment of patients with nAMD or DME, even with these upcoming treatment algorithms, strategies that strengthen patient adherence will become more important. The high user satisfaction and increased testing frequency observed with the use of MacuFix® may lead to improved outcomes in the treatment of macular disease.

References:

1. Amsler M. Die Untersuchung des qualitativen Sehens mit dem quadratischen Netz. Anweisung zum Gebrauch der Testtafeln. : Theodore Hamblin LTD; 1958.

2. Arimura E, Matsumoto C, Okuyama S, Takada S, Hashimoto S, Shimomura Y. Quantification of metamorphopsia in a macular hole patient using M-CHARTS. Acta Ophthalmol Scand. 2007;85(1):55-9.

3. Chew EY, Clemons TE, Bressler SB, Elman MJ, Danis RP, Domalpally A, et al. Randomized trial of a home monitoring system for early detection of choroidal neovascularization home monitoring of the Eye (HOME) study. Ophthalmology. 2014;121(2):535-44.

4. Coco-Martin RM, Pichel-Mouzo M, Fernandez I, Plata-Cordero M, Lopez-Miguel A. Reliability of colour perimetry to assess macular pigment optical density in age-related macular degeneration. Eur J Ophthalmol. 2020;30(6):1480-6.

5. Welker SG, Pfau M, Heinemann M, Schmitz-Valckenberg S, Holz FG, Finger RP. Retest Reliability of Mesopic and Dark-Adapted Microperimetry in Patients With Intermediate Age-Related Macular Degeneration and Age-Matched Controls. Invest Ophthalmol Vis Sci. 2018;59(4):152-9.

6. Ward E, Wickens RA, O'Connell A, Culliford LA, Rogers CA, Gidman EA, et al. Monitoring for neovascular age-related macular degeneration (AMD) reactivation at home: the MONARCH study. Eye (Lond). 2020.

7. Claessens D, Schuster AK. Correlation of Quantitative Metamorphopsia Measurement and Central Retinal Thickness in Diabetic Macular Edema and Age-Related Exsudative Macular Degeneration. Klin Monbl Augenheilkd. 2019;236(7):877-84.

8. Claessens D, Schuster AK, Krüger RV, Liegl M, Singh L, Kirchhof B. Test-Retest-Reliability of Computer-Based Metamorphopsia Measurement in Macular Diseases. Klin Monbl Augenheilkd. 2020 Dec. 7.(Epub ahead of print)

9. Bangor A, Kortum PT, Miller JT. An Empirical Evaluation of the System Usability Scale. International Journal of Human-Computer Interaction. 2008;24(6):574-94.

10. Brooke J. SUS-A quick and dirty usability scale. In: Corporation DE, editor. Usability Evaluation In Industry. London: CRC Press; 1996.

11. Muether PS HR, Hermann MM, Kirchhof B, Fauser S. Long-term effects of ranibizumab treatment delay in neovascular age-related macular degeneration. Graefes Arch Clin Exp Ophthalmol 2013(251):453–8.

12. Lim JH, Wickremasinghe SS, Xie J, Chauhan DS, Baird PN, Robman LD, et al. Delay to treatment and visual outcomes in patients treated with anti-vascular endothelial growth factor for age-related macular degeneration. Am J Ophthalmol. 2012;153(4):678-86.

13. Framme C, Eter N, Hamacher T, Hasanbasic Z, Jochmann C, Johnson KT, et al. Aflibercept for Patients with Neovascular Age-Related Macular Degeneration in Routine Clinical Practice in Germany: Twelve-Month Outcomes of PERSEUS. Ophthalmol Retina. 2018;2(6):539-49.

14. Wintergerst MWM, Bouws J, Loss J, Heimes B, Pauleikhoff D, Holz FG, et al. Reasons for delayed and discontinued therapy in age-related macular degeneration. Ophthalmologe. 2018;115(12):1035-41.

15. Achard OA, Safran AB, Duret FC, Ragama E. Role of the completion phenomenon in the evaluation of Amsler grid results. Am J Ophthalmol. 1995;120(3):322-9.

16. Parkes L, Lund J, Angelucci A, Solomon JA, Morgan M. Compulsory averaging of crowded orientation signals in human vision. Nat Neurosci. 2001;4(7):739-44.

17. Domalpally A, Clemons TE, Bressler SB, Danis RP, Elman M, Kim JE, et al. Imaging Characteristics of Choroidal Neovascular Lesions in the AREDS2-HOME Study: Report Number 4. Ophthalmol Retina. 2019;3(4):326-35.

18. Ehlken C, Helms M, Bohringer D, Agostini HT, Stahl A. Association of treatment adherence with real-life VA outcomes in AMD, DME, and BRVO patients. Clin Ophthalmol. 2018;12:13-20.

19. Holz FG, Tadayoni R, Beatty S, Berger AR, Cereda MG, Hykin P, et al. Determinants of visual acuity outcomes in eyes with neovascular AMD treated with anti-VEGF agents: an instrumental variable analysis of the AURA study. Eye (Lond). 2016;30(8):1063-71.

20. Holz FG, Tadayoni R, Beatty S, Berger A, Cereda MG, Cortez R, et al. Multi-country real-life experience of anti-vascular endothelial growth factor therapy for wet age-related macular degeneration. Br J Ophthalmol. 2015;99(2):220-6.

21. Ulbig M, Höh H, Schmickler S, Wolf A, Dimopoulos S, Lorenz K, et al. Treatment reality with ranibizumab in clinical routine use for patients with diabetic macular edema : 1-year results of the German POLARIS cohort. Ophthalmologe 2019;116(7):631-9.

22. Holz FG, Johnson KT, Bauer-Steinhusen U, Rech C, Machewitz T, Muller S, et al. ANDROMEDA-an investigation of factors influencing the adherence of patients with neovascular age-related macular degeneration using the newly developed patient questionnaire LAF-IVT. Ophthalmologe. 2019;117(8):765-74.

23. Carrasco J, Pietsch GA, Nicolas MP, Koerber C, Bennison C, Yoon J. Real-World Effectiveness and Real-World Cost-Effectiveness of Intravitreal Aflibercept and

Intravitreal Ranibizumab in Neovascular Age-Related Macular Degeneration: Systematic Review and Meta-Analysis of Real-World Studies. Adv Ther. 2020;37(1):300-15.

24. Angermann R, Rauchegger T, Nowosielski Y. Treatment compliance and adherence among patients with diabetic retinopathy and age-related macular degeneration treated by anti-vascular endothelial growth factor under universal health coverage. Graefes Arch Clin Exp Ophthalmol. 2019;257(10):2119-25.

25. Parikh R, Avery RL, Saroj N, Thompson D, Freund KB. Incidence of New Choroidal Neovascularization in Fellow Eyes of Patients With Age-Related Macular Degeneration Treated With Intravitreal Aflibercept or Ranibizumab. JAMA Ophthalmol. 2019; 137(8):914-20.

26. Heier JS, Brown DM, Chong V, Korobelnik JF, Kaiser PK, Nguyen QD, et al. Intravitreal aflibercept (VEGF trap-eye) in wet age-related macular degeneration. Ophthalmology. 2012;119(12):2537-48.

27. Krüger R, Claessens D. Reliability of a Novel Computer-Based Metamorphopsia Categorization Tool. Association for Research and Vision in Ophthalmology; Baltimore 2020.

Figure legends:

Figure 1: MacuFix used on a Smartphone

Table Legend:

Table 1: Average values of individual questions in the SUS questionnaire

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Question number and text of the question	Average value
1. I can well imagine using the test regularly.	2,8
2. I find the test unnecessarily complicated.	3,1
3. I find the test easy to use.	3,0
4. I think I would need technical support to use the test.	3,1
5. I find that the various functions of the test are easy to use.	2,8
6. I think that there are too many inconsistencies in the test.	2,6
7. I can imagine that most people learn to master the test quickly.	3,3
8. I find the operation very complicated.	3,4
9. I felt very confident in using the test.	3,2
10. I had to learn a lot of things before I could work with the test.	3,4